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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 02-076)

PATENT

In re Application of: Elliott et al.

Serial No.: 10/076,260

Filed: February 14, 2002

For: G-Protein Coupled Receptor  
Molecules and Uses Thereof

Before the Examiner: F. Hamud

Group Art Unit: 1647

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

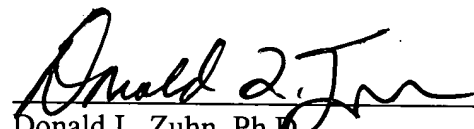
**TRANSMITTAL LETTER**

1. We are transmitting herewith the attached papers for the above-described patent application:  
Response to Restriction Requirement and return postcard.
2. GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES: Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2490.
3. CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8: The undersigned hereby certifies that this Transmittal Letter and the papers, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 26, 2004.

Respectfully submitted,  
McDonnell Boehnen Hulbert & Berghoff

Dated: April 26, 2004

By:

  
Donald L. Zuhn, Ph.D.  
Reg. No. 48,710



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 02-076)

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In re Application of:	Elliott et al.	)	
		)	
Serial No.:	10/076,260	)	Before the Examiner: F. Hamud
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For:	G-Protein Coupled Receptor	)	
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Sir:

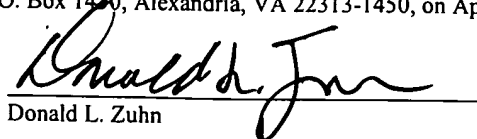
**RESPONSE TO RESTRICTION REQUIREMENT MAILED MARCH 25, 2004**

Responsive to the Restriction Requirement mailed March 25, 2004, Applicants elect to prosecute claims 1-8, 10, 11, 43-45, 56, and 57, designated as the invention of Group I by the Action, which the Action states are drawn to an isolated nucleic acid molecule comprising a specific nucleotide sequence. The Action also asserts that the claims of Group I-X recite a multitude of nucleic acid sequences and polypeptide sequences that constitutes a recitation of an implied, mis-joined Markush group containing multiple independent and distinct inventions, and that each of the nucleic acids is independent and distinct because no common structural or functional properties are shared. To the extent that Applicants understand this assertion, Applicants elect to prosecute claims directed to nucleic acid molecules encoding human GPCR polypeptides, with traverse.

Applicants first request clarification regarding the Action's assertion that the claims of Group I-X recite a multitude of nucleic acid sequences and polypeptide sequences that constitutes a recitation of an implied, mis-joined Markush group containing multiple independent and distinct inventions, and that each of the nucleic acids is independent and distinct because no common structural or functional properties are shared. Assuming that Applicants have correctly interpreted

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Donald L. Zuhn

the instant Action as requiring an election of a genus of nucleic acid molecules encoding human, murine, or rat GPCR polypeptides, Applicants elect to prosecute claims directed to nucleic acid molecules encoding human GPCR polypeptides (*i.e.*, the nucleic acid molecule of SEQ ID NO: 1, nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2, and nucleic acid molecules encoding variants and fragments of the polypeptide of SEQ ID NO: 2), with traverse. The basis for Applicants' traversal of the requirement is as follows. Applicants respectfully submit that because the genus of nucleic acid molecules encoding human, murine, and rat GPCR polypeptides shares common structural properties and substantial amino acid identity and similarity, the members of this genus do not constitute multiple independent and distinct inventions.

Applicants note that the instant application teaches nucleic acid molecules encoding human, murine, and rat GPCR polypeptides, and contend that in view of the substantial amino acid identity and similarity shared by these polypeptides (Exhibit A), one of ordinary skill in the art would clearly recognize that the human, murine, and rat GPCR polypeptides taught in the instant application are orthologs. Applicants also note that the human and murine GPCR polypeptides taught in the instant application share 78% identity and 85% similarity (Exhibit B), the human and rat GPCR polypeptides share 78% identity and 86% similarity (Exhibit C), and the murine and rat GPCR polypeptides share 90% identity and 93% similarity. Moreover, as disclosed in Figure 4 of the instant application, the human, murine, and rat GPCR polypeptides also share common structural properties in that each protein possesses seven transmembrane domains. The ClustalW sequence alignments shown in Exhibits B-D were performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; <http://www.accelrys.com>) at the default settings.

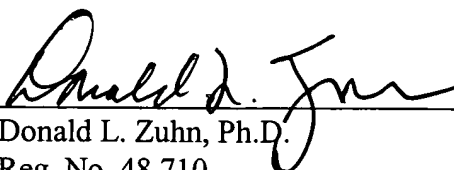
Applicants respectfully submit that because the genus of nucleic acid molecules encoding human, murine, and rat GPCR polypeptides taught in the instant application shares substantial sequence identity and similarity, and therefore, share, rather than lack, common structural properties, the members of this genus do not constitute multiple independent and distinct inventions. Applicants, therefore, respectfully request examination of claims directed to nucleic acid molecules encoding human, murine, and rat GPCR polypeptides.

Applicants do not believe that any additional fee is required. However, the Commissioner is authorized to charge any deficiency to Deposit Account No. 13-2490. If Examiner Hamud believes

it to be helpful, the Examiner is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,  
**McDonnell Boehnen Hulbert & Berghoff**

Dated: April 26, 2004

By:   
Donald L. Zuhn, Ph.D.  
Reg. No. 48,710

# EXHIBIT A

		10		20		30																										
hUGPCR			M	Y	N	G	S	C	C	R	I	E	G	D	T	I	S	Q	V	M	P	P	L	L								
mutPCR	M	P	V	L	S	P	T	A	M	D	N	G	S	C	C	L	I	E	G	E	P	I	S	Q	V	M	P	P	L	L		
rsGPCR	M	L	F	L	S	P	S	A	M	D	N	G	S	C	C	L	I	E	G	E	P	I	T	Q	V	M	P	P	L	L		
	M			L	S	P	.	A	M	D	N	G	S	C	C	L	I	E	G	E	P	I	S	Q	V	M	P	P	L	L		
			40																													
hUGPCR			I	V	A	F	V	L	G	A	L	G	N	G	V	A	L	G	G	F	C	F	H	M	K	T	V	K	P	S	T	V
mutPCR			I	L	V	F	V	L	G	A	L	G	N	G	I	A	L	G	G	F	C	F	H	M	K	T	V	K	S	S	T	I
rsGPCR			I	L	A	F	L	L	G	A	L	G	N	G	L	A	L	G	G	F	C	F	H	M	K	T	V	K	S	S	T	I
			I	L	A	F	V	L	G	A	L	G	N	G	.	A	L	G	G	F	C	F	H	M	K	T	V	K	S	S	T	I
			70																													
hUGPCR			Y	L	F	N	L	A	V	A	D	F	L	M	I	C	L	P	F	R	T	D	Y	Y	L	R	R	R	H	V	A	
mutPCR			Y	L	F	N	L	A	V	A	D	F	L	M	I	C	L	P	L	R	T	D	Y	Y	L	R	R	R	H	V	I	
rsGPCR			Y	L	F	N	L	A	V	A	D	F	L	M	I	C	L	P	L	R	T	D	Y	Y	L	R	R	R	H	V	I	
			Y	L	F	N	L	A	V	A	D	F	L	M	I	C	L	P	L	R	T	D	Y	Y	L	R	R	R	H	W	I	
			100																													
hUGPCR			F	G	D	I	P	C	R	V	G	L	F	T	L	A	M	N	R	A	G	S	I	V	F	L	T	V	V	A	A	D
mutPCR			F	G	D	I	A	C	R	L	V	L	F	K	L	A	M	N	R	A	G	S	I	V	F	L	T	V	V	A	V	D
rsGPCR			L	G	D	I	P	C	R	L	V	L	F	M	L	A	M	N	R	A	G	S	I	V	F	L	T	V	V	A	V	D
			F	G	D	I	P	C	R	L	V	L	F		L	A	M	N	R	A	G	S	I	V	F	L	T	V	V	A	V	D
			130																													
hUGPCR			R	Y	F	K	V	V	H	P	H	H	A	V	N	I	S	T	R	V	A	A	G	I	V	G	T	L	V	A	L	
mutPCR			R	Y	F	K	V	V	H	P	H	H	M	V	N	A	I	S	N	R	T	A	A	A	T	A	C	V	L	V	T	L
rsGPCR			R	Y	F	K	V	V	H	P	H	H	M	V	N	A	I	S	N	R	T	A	A	A	I	V	C	V	L	V	T	L
			R	Y	F	K	V	V	H	P	H	H	M	V	N	A	I	S	N	R	T	A	A	A	I	V	C	V	L	W	T	L
			160																													
hUGPCR			V	I	L	G	T	V	Y	L	L	L	E	N	H	L	G	V	Q	E	T	A	V	S	C	E	S	F	I	M	E	S
mutPCR			V	I	L	G	T	V	Y	L	L	M	E	S	H	L	G	V	Q	G	T	L	S	S	C	E	S	F	I	M	E	S
rsGPCR			V	I	L	G	T	V	Y	L	L	M	E	S	H	L	G	V	R	G	M	V	S	S	C	E	S	F	I	M	E	S
			V	I	L	G	T	V	Y	L	L	M	E	S	H	L	C	V	Q	G	T	.	S	S	C	E	S	F	I	M	E	S

	190	200	210
hUGPCR	ANGVHDI MFQLEFFMPLGIILFCSEFKIVWS		
muGPCR	ANGVHDV MFQLEFFLPLTIILFCSEVN VVWS		
rsGPCR	ANGVHDI MFQLEFFLPLTIILFCSEFKVVWS		
	ANGVHDI MFQLEFFLPLTIILFCSEFKVVWS		

	220	230	240
hUGPCR	LRRRQQQLARQARMKKATRFIMVVAIVFITC		
muGPCR	LRRRQQQLTRQARMRRATRFIMVVASVFITC		
rsGPCR	LRQRQQQLTRQARMRRATRFIMVVASVFITC		
	LRRRQQQLTRQARMRRATRFIMVVASVFITC		

	250	260	270
hUGPCR	YLPSSVSA RLYFLWTPSSACDPSVHGALHI		
muGPCR	YLPSSVLARLYFLWTPISACDPSVHTALHV		
rsGPCR	YLPSSVLARLYFLWTPSSACDPSVHIALHV		
	YLPSSVLARLYFLWTPSSACDPSVHIALHV		

	280	290	300
hUGPCR	TLSFTYMN NSMLDPLVYYFSSSPSPKFFYNKL		
muGPCR	TLSFTYLN NSMLDPLVYYFSSSPSLPKFFYAKL		
rsGPCR	TLSLTLYLN NSMLDPLVYYFSSSPSPKFFYAKL		
	TLSFTYLN NSMLDPLVYYFSSSPSPKFFYAKL		

	310	320	330
hUGPCR	KICSLKPKQPGHSKTQRPEEMPISNLGRSS		
muGPCR	TICSLKPKRPGRTRRSEEMPISNLCSSKS		
rsGPCR	KIRSLKPRRPGRSQARRSEEMPISNLCRKS		
	KICSLKPKRPGRSKTRRSEEMPISNLCRKS		

	340	350	360
hUGPCR	CISVANSEFQSQSDGQWDPHIV EWH		
muGPCR	SIDGANRSQRPSDGQWDLQVC		
rsGPCR	STDVVNSSQRPSDGQWGLQVC		
	SIDVANSSQRPSDGQWDLQVCEWH		

## EXHIBIT B

## 1. huGPCR vs. muGPCR

Aligned Length = 354      Gaps = 0  
Identities = 276 (78%)      Similarities = 26 (7%)

huGPCR	1	MYNGSCCRIEGDTISQVMPPLLLIVFVLGALGNGVALCGFCF	42
muGPCR	1	MPVLSPTAMDNGSCCLIEGEPISQVMPPLLLILFVLGALGNGIALCGFCF	50
		* * * * *	
huGPCR	43	HMKTWKPSTVYLFNLAVADFLLMICLPFRTDYYLRRRRHWAFGDIPCRVGL	92
muGPCR	51	HMKTWKSSTIYLFNLAVADFLLMICLPFRTDYYLRRRRHWIFGDIACRLVL	100
		* * * * *	
huGPCR	93	FTLAMNRAGSIVFLTVVAADRYFKVVHPHHAVENTISTRVAAGIVCTLWAL	142
muGPCR	101	FKLAMNRAGSIVFLTVVAVDRYFKVVHPHMHVNAISNRTAAATACVLWTL	150
		* * * * *	
huGPCR	143	VILGTVYLLLENHLCVQETAVSCSEFIMESANGWHDIMFQLEFFMPLGII	192
muGPCR	151	VILGTVYLLMESHLCVQGTLSSEFIMESANGWHDVMFQLEFFLPLTII	200
		* * * * *	
huGPCR	193	LFCSFKIIVWSLRRRQQLARQARMKKATRFIMVVAIVFITCYLPSVSARLY	242
muGPCR	201	LFCSVNVWSLRRRQQLTRQARMRRATRFIMVVASVFITCYLPSVLARLY	250
		* * * * *	
huGPCR	243	FLWTVPSSACDPSVHGALHITLSFTYMNSMLDPLVYYFSSPSFPKFYNKL	292
muGPCR	251	FLWTVPTSACDPSVHTALHVTLSTYLNMSMLDPLVYYFSSPSLPKFYAKL	300
		* * * * *	
huGPCR	293	KICSLKPKQPGHSKTORPEEMPISNLGRRSCISVANSFQSQSDGQWDPHI	342
muGPCR	301	TICSLKPKRPGRTKTRSEEMPISNLCSKSSIDGANRSQRPSDGQWDLQV	350
		* * * * *	
huGPCR	343	VEWH	346
muGPCR	351	C	351



## EXHIBIT C

### 2. huGPCR vs. raGPCR

Aligned Length = 354    Gaps = 0  
Identities = 276 (78%)    Similarities = 30 (8%)

```
huGPCR   1      MYNGSCCRIEGDTISQVMPPLLIVAFVLGALGNGVALCGFCF  42
raGPCR   1 MLFLSPSAMDNGSCCLIEGEPITQVMPPLLILAFLLGALGNGLALCGFCF  50
          * ***** ** . *.*****.***.*****.*****

huGPCR   43 HMKTWKPSTVYLFNLAVADFLLMICLPFRTDYLLRRRHWAFGDIPCRVGL  92
raGPCR   51 HMKTWKSSTIYLFNLAVADFLLMICLPLRTDYLLRRRHWILGDIPCRLVL 100
          ***** ** .*****.*****.*****.*****. *

huGPCR   93 FTLAMNRAGSIVFLTVVAADRYFKVVPHPHAVNTISTRVAAGIVCTLWAL 142
raGPCR  101 FMLAMNRAGSIVFLTVVAVDRYFKVVPHPHMVNAISNRTAAAIVCVLWTL 150
          * *****.*****.*****.***.***.***.***.***

huGPCR  143 VILGTVYLLLENHLCVQETAVSCSFIMESANGWHDIMFQLEFFMPLGII 192
raGPCR  151 VILGTVYLLMESHLCVRGMVSSCSFIMESANGWHDIMFQLEFFLPLTII 200
          *****.* ****. *****.*****.*** **

huGPCR  193 LFCSFKIVWSLRRRQQLARQARMKKATRFIMVVAIVFITCYLPSVSARLY 242
raGPCR  201 LFCSFKVWWSLRQRQQLTRQARMRRATRFIMVVASVFITCYLPSVLARLY 250
          *****.*****.*****.*****.*****.*****.*****

huGPCR  243 FLWTVPSSACDPSVHGALHITLSFTYMNSMLDPLVYYFSSPSFPKFYNKL 292
raGPCR  251 FLWTVPSSACDPSVHIALHVTLSTLYLNSMLDPLVYYFSSPSFPKFYAKL 300
          *****.*****.***.*** ** .*****.*****.***** **

huGPCR  293 KICSLKPKQPGHSKTQRPEEMPISNLGRRSCISVANSFQSQSDGQWDPHI 342
raGPCR  301 KIRSLKPRRPGRSQARRSEEMPISNLCRKSSTDVVNSSQRPSDGQWGLQV 350
          ** *****.***.***.***.*****.***.***.***.*** **

huGPCR  343 VEWH 346
raGPCR  351 C 351
```

## EXHIBIT D

### 3. muGPCR vs. raGPCR

Aligned Length = 351    Gaps = 0  
Identities = 316 (90%)    Similarities = 13 (3%)

```
muGPCR   1 MPVLSPTAMDNGSCCLIEGEPISQVMPPLLILVFLGALGNGIALCGFCF  50
raGPCR   1 MLFLSPSAMDNGSCCLIEGEPITQVMPPLLILAFLLGALGNGIALCGFCF  50
          *   ***.*****.*****.***** * .*****.*****

muGPCR   51 HMKTWKSSTIYLFNLAVADFLLMICLPLRTDYLLRRRHWFIDGDIACRLVL 100
raGPCR   51 HMKTWKSSTIYLFNLAVADFLLMICLPLRTDYLLRRRHWFIDGDIACRLVL 100
          *****

muGPCR  101 FKLAMNRAGSIVFLTVVAVDRYFKVVHPHMHVNAISNRTAAATACVLWTL 150
raGPCR  101 FKLAMNRAGSIVFLTVVAVDRYFKVVHPHMHVNAISNRTAAATACVLWTL 150
          * *****

muGPCR  151 VILGTVYLLMESHLCVQGTLSSECFIMESANGWHDVDFQLEFFLPLTII 200
raGPCR  151 VILGTVYLLMESHLCVQGTLSSECFIMESANGWHDVDFQLEFFLPLTII 200
          *****

muGPCR  201 LFCSVNVVWSLRRRQQLTRQARMRRATRFIMVVASVFITCYLPSVLARLY 250
raGPCR  201 LFCSVNVVWSLRRRQQLTRQARMRRATRFIMVVASVFITCYLPSVLARLY 250
          *****

muGPCR  251 FLWTVPTSACDPSVHTALHVTLSFTYLNMLDPLVYFSSPSLPKFYAKL 300
raGPCR  251 FLWTVPTSACDPSVHTALHVTLSFTYLNMLDPLVYFSSPSLPKFYAKL 300
          *****

muGPCR  301 TICSLKPKRPGRTKTRRSEEMPISNLCSKSSIDGANRSQRPSDGQWDLQV 350
raGPCR  301 KIRSLKPKRPGRSQARRSEEMPISNLCSKSSIDGANRSQRPSDGQWDLQV 350
          * ****.*****.***** ***** * * *****

muGPCR  351 C 351
raGPCR  351 C 351
          *
```